

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS
CENTRAL DIVISION**

ABBOTT GMBH & CO., KG; and ABBOTT
BIORESEARCH CENTER, INC.

Plaintiffs,

v.

CENTOCOR ORTHO BIOTECH, INC.

Defendant.

Civil Action No. 4:09-cv-11340-FDH

Jury Trial Demanded

**DEFENDANT'S AMENDED AND SUPPLEMENTED PRELIMINARY INVALIDITY
AND NON-INFRINGEMENT CONTENTIONS**

Pursuant to Local Rules 16.1 and 16.6, Defendant Centocor Ortho Biotech, Inc. (“Centocor”) hereby makes the following Amended and Supplemented Preliminary Invalidity and Non-Infringement Contentions.

Discovery has just begun, and the Preliminary Contentions herein are based on information and documents currently available to Centocor. Centocor reserves the right to amend and/or supplement these Preliminary Contentions, including as set forth by the March 2, 2010 Scheduling Order. Centocor also reserves the right to rely on additional evidence to support its Preliminary Contentions.

I. Preliminary Invalidity Contentions

A. Obviousness

Each of the asserted claims of U.S. Patent No. 6,914,128 (the “128 patent”) and U.S. Patent No. 7,504,485 (the “485 patent”) are obvious over the combinations of references set forth in the following chart:

128 Patent	
1. An isolated human antibody, or antigen binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.	<p>Obvious over the combination of one or more of the following:</p> <p>U.S. Patent No. 5,811,523 (Trinchieri et al.)</p> <p>U.S. Patent No. 5,780,597 (Gately et al.)</p> <p>U.S. Patent No. 6,054,487 (Sekut et al.)</p> <p>PCT Publication WO98/41232 (Sekut et al.)</p> <p>U.S. Patent No. 6,150,584 (Kucherlapati et al.)</p> <p>U.S. Patent No. 6,673,986 (Kucherlapati et al.)</p> <p>PCT Publication WO94/002602 (Kucherlapati et al.)</p> <p>PCT Publication WO96/33735 (Kucherlapati et al.)</p>

	<p>PCT Publication WO96/34096 (Kucherlapati et al.)</p> <p>Chizzonite et al., J. Immunol. 147:1548 (1991)</p> <p>Valiente et al., Cellular Immunology 145:187 (1992)</p> <p>Trinchieri, Ann. Rev. Immunol., 13:251 (1995)</p> <p>Meager et al., Lancet 350, 1596 (1997)</p> <p>Beeson et al., Ann. NY Acad. Sci. 841:371 (1998)</p> <p>in combination with known methods for creating isolated, recombinant, high-affinity, neutralizing human antibodies, including against human self antigens, and for increasing the affinity of those human antibodies, as set forth, for example in the following:</p> <p>U.S. Patent No. 5,545,807 (Surani et al.)</p> <p>U.S. Patent No. 5,625,126 (Lonberg et al.)</p> <p>U.S. Patent No. 5,770,429 (Lonberg et al.)</p> <p>U.S. Patent No. 6,300,129 (Lonberg et al.)</p> <p>U.S. Patent No. 6,255,458 (Lonberg et al.)</p> <p>U.S. Patent No. 7,084,260 (Lonberg et al.)</p> <p>PCT Publication WO98/24884 (Lonberg et al.)</p> <p>PCT Publication WO97/13852 (Lonberg et al.)</p> <p>PCT Publication WO94/25585 (Lonberg et al.)</p> <p>PCT Publication WO98/50433 (Jakobovits et al.)</p> <p>PCT Publication WO98/24893 (Jakobovits et al.)</p> <p>Lonberg et al., Nature 368:856 (1994)</p> <p>Lonberg et al., Int. Rev. Immunol. 13:65 (1995)</p> <p>Taylor et al., Int. Immunol. 6:579 (1994)</p> <p>Green et al., Nature Genetics 7:12 (1994)</p>
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	Wagner et al., Eur. J. Immunol. 24:2672 (1994)
	Wagner et al., Nucl. Acids Res. 22:1389 (1994)
	Harding et al., Ann. NY Acad. Sci. 764:536 (1995)
	Jakobovits, Curr. Op. Biotechnol. 6:561 (1995)
	Bruggemann et al., Immunol. Today 17:391 (1996)
	Fishwild et al., Nature Biotechnology 14:845 (1996)
	Zou et al., FASEB J. 10:1227 (1996)
	Mendez et al., Nature Genetics 15:146 (1997)
	Neuberger et al., Nature 386:25 (1997)
	Bruggemann et al., Curr. Op. Biotechnol.. 8:455 (1997)
	U.S. Patent No. 5,652,138 (Burton et al.)
	U.S. Patent No. 5,804,440 (Burton et al.)
	U.S. Patent No. 5,910,486 (Curiel et al.)
	U.S. Patent No. 6,284,471 (Le et al.)
	U.S. Patent No. 5,919,452 (Le et al.)
	U.S. Patent No. 5,656,272 (Le et al.)
	U.S. Patent No. 5,698,195 (Le et al.)
	U.S. Patent No. 6,277,969 (Le et al.)
	Jespers et al., Nature Biotechnology 12:899 (1994)
	Burton et al. Adv. Immunol. 57:191 (1994)
	Griffiths et al., EMBO J. 13:3245 (1994)
	Vaughan et al., Nature Biotechnology 14:309 (1996)
	Schier et al., J. Mol. Biol. 263:551 (1996)
	Barbas et al., Trends Biotechnol. 14:230 (1996)
	Hoogenboom, Trends Biotechnol. 15:62 (1997)

	Rader et al., Curr. Op. Biotechnol. 8:503 (1997) Sheets et al., PNAS 95:6157 (1998)
2. The isolated human antibody of claim 1, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} \text{ s}^{-1}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
3. The isolated human antibody of claim 1, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} \text{ s}^{-1}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
4. The isolated human antibody of claim 1, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of $1.34 \times 10^{-10} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
5. The isolated human antibody of claim 1, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of $9.74 \times 10^{-11} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
6. The isolated human antibody, or an antigen-binding portion thereof, of claim 1, which is a recombinant antibody, or antigen-binding portion thereof.	Obvious over the same combinations as claim 1 of the 128 patent.
7. The isolated human antibody of any one of claims 1 to 3, wherein the antibody is a neutralizing antibody.	Obvious over the same combinations as claim 1 of the 128 patent.
8. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast	Obvious over the same combinations as claim 1 of the 128 patent.

proliferation in an in vitro PHA assay with an IC_{50} of $1 \times 10^{-9} M$ or less.	
9. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of $1 \times 10^{-10} M$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
10. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of $1 \times 10^{-11} M$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
11. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro phytohemagglutinin blast proliferation assay (PHA assay) with an IC_{50} of $1 \times 10^{-7} M$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
12. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA, assay with an IC_{50} of $1 \times 10^{-8} M$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
13. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of $1 \times 10^{-10} M$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
14. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an	Obvious over the same combinations as claim 1 of the 128 patent.

IC ₅₀ of 1×10^{-11} M or less.	
15. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC ₅₀ of 5×10^{-12} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
27. An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K _d of 1×10^{-10} M or less and binds to an epitope on the p40 subunit of human IL-12.	Obvious over the same combinations as claim 1 of the 128 patent.
28. The isolated human antibody of claim 27, which neutralizes the activity of human IL-12.	Obvious over the same combinations as claim 1 of the 128 patent.
29. A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K _{off} rate constant of $1 \times 10^{-2} \text{s}^{-1}$ or less, as determined by surface plasmon resonance.	Obvious over the same combinations as claim 1 of the 128 patent.
30. The neutralizing isolated human antibody of claim 29, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k _{off} rate constant of $1 \times 10^{-4} \text{s}^{-1}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
31. The neutralizing isolated human antibody of claim 29, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k _{off} rate constant of $1 \times 10^{-5} \text{s}^{-1}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
32. The neutralizing isolated human antibody of claim 29, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K _{off} rate constant of $1 \times 10^{-}$	Obvious over the same combinations as claim 1 of the 128 patent.

3 s^{-1} or less.	
33. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} or $1 \times 10^{-7} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
34. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} or $1 \times 10^{-8} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
35. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} or $1 \times 10^{-9} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
36. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} or $1 \times 10^{-10} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
37. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} or $1 \times 10^{-11} \text{ M}$ or less.	Obvious over the same combinations as claim 1 of the 128 patent.
38. The neutralizing isolated	Obvious over the same combinations as claim 1 of the 128

human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC ₅₀ or 1x10 ⁻¹⁰ M or less.	patent.
39. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC ₅₀ or 1x10 ⁻¹¹ M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
40. The neutralizing isolated human antibody of any one of claims 29 to 31 and 32, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC ₅₀ or 5x10 ⁻¹² M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
50. An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K _d of 1.34x10 ⁻¹⁰ M or less, and neutralizes human IL-12.	Obvious over the same combinations as claim 1 of the 128 patent.
51. The isolated human antibody of claim 50, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K _d of 9.74x10 ⁻¹¹ M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
52. The isolated human antibody, or antigen-binding portion thereof, of claim 50 or 51, which is a recombinant antibody, or antigen-binding portion thereof.	Obvious over the same combinations as claim 1 of the 128 patent.
53. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA	Obvious over the same combinations as claim 1 of the 128 patent.

assay with an IC_{50} of 1×10^{-7} M or less.	
54. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of 1×10^{-8} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
55. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of 1×10^{-9} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
56. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of 1×10^{-10} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
57. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of 1×10^{-11} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
58. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
59. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-11} M or less.	Obvious over the same combinations as claim 1 of the 128 patent.

60. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC ₅₀ of 5x10 ⁻¹² M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
61. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC ₅₀ of 1x10 ⁻⁹ M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
62. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC ₅₀ of 1x10 ⁻¹⁰ M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
63. The isolated human antibody of claim 52, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC ₅₀ of 1x10 ⁻¹¹ M or less.	Obvious over the same combinations as claim 1 of the 128 patent.
64. A pharmaceutical composition comprising the antibody or an antigen binding portion thereof of claims 1, 16, 21, 27, 29, 41, 44, 45, 48, 50, or 51, and a pharmaceutically acceptable carrier.	Obvious over the same combinations as claim 1 of the 128 patent.
70. A pharmaceutical composition comprising the antibody or antigen binding portion thereof of claim 7, and a pharmaceutically acceptable carrier.	Obvious over the same combinations as claim 1 of the 128 patent.
485 patent	
1. A pharmaceutical composition comprising an isolated human antibody, or antigen-binding	Obvious over the combination of one or more of the following:

<p>portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12, and further comprising an additional agent.</p>	<p>U.S. Patent No. 5,811,523 (Trinchieri et al.)</p> <p>U.S. Patent No. 5,780,597 (Gately et al.)</p> <p>U.S. Patent No. 6,054,487 (Sekut et al.)</p> <p>PCT Publication WO98/41232 (Sekut et al.)</p> <p>U.S. Patent No. 6,150,584 (Kucherlapati et al.)</p> <p>U.S. Patent No. 6,673,986 (Kucherlapati et al.)</p> <p>PCT Publication WO94/002602 (Kucherlapati et al.)</p> <p>PCT Publication WO96/33735 (Kucherlapati et al.)</p> <p>PCT Publication WO96/34096 (Kucherlapati et al.)</p> <p>Chizzonite et al., J. Immunol. 147:1548 (1991)</p> <p>Valiente et al., Cellular Immunology 145:187 (1992)</p> <p>Trinchieri, Ann. Rev. Immunol., 13:251 (1995)</p> <p>Meager et al., Lancet 350, 1596 (1997)</p> <p>Beeson et al., Ann. NY Acad. Sci. 841:371 (1998)</p>
<p>2. The composition of claim 1, wherein the antibody, or antigen-binding portion thereof, is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to the p35 subunit of IL-12.</p>	<p>Obvious over the same combinations as claim 1 of the 485 patent.</p>
<p>3. The composition of claim 1, wherein the antibody, or antigen-binding portion thereof, is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to a p19 subunit.</p>	<p>Obvious over the same combinations as claim 1 of the 485 patent.</p>
<p>4. The composition of claim 1, wherein the antibody, or antigen-binding portion thereof, is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to the p35 subunit of IL-12</p>	<p>Obvious over the same combinations as claim 1 of the 485 patent.</p>

and when the p40 subunit is bound to a p19 subunit.	
6. The composition of claim 1, wherein the antibody, or antigen-binding portion thereof, is further capable of binding to a first heterodimer and is also capable of binding to a second heterodimer, wherein the first heterodimer comprises the p40 subunit of IL-12 and the p35 subunit of IL-12, and wherein the second heterodimer comprises the p40 subunit of IL-12 and a p19 subunit.	Obvious over the same combinations as claim 1 of the 485 patent.
7. The composition of claim 6, wherein the antibody, or antigen-binding portion thereof, neutralizes a biological activity of the first heterodimer.	Obvious over the same combinations as claim 1 of the 485 patent.
8. The composition of claim 6, wherein the antibody, or antigen-binding portion thereof, neutralizes a biological activity of the second heterodimer.	Obvious over the same combinations as claim 1 of the 485 patent.
9. The composition of claim 6, wherein the antibody, or antigen-binding portion thereof, neutralizes a biological activity of the first heterodimer and the second heterodimer.	Obvious over the same combinations as claim 1 of the 485 patent.
10. The composition of claim 7 or 9, wherein the antibody, or antigen binding portion thereof, inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC_{50} of 1×10^{-9} M or less, or which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.	<p>Obvious over the combination of one or more of the following:</p> <p>U.S. Patent No. 5,811,523 (Trinchieri et al.)</p> <p>U.S. Patent No. 5,780,597 (Gately et al.)</p> <p>U.S. Patent No. 6,054,487 (Sekut et al.)</p> <p>PCT Publication WO98/41232 (Sekut et al.)</p> <p>U.S. Patent No. 6,150,584 (Kucherlapati et al.)</p>

	<p>U.S. Patent No. 6,673,986 (Kucherlapati et al.)</p> <p>PCT Publication WO94/002602 (Kucherlapati et al.)</p> <p>PCT Publication WO96/33735 (Kucherlapati et al.)</p> <p>PCT Publication WO96/34096 (Kucherlapati et al.)</p> <p>Chizzonite et al., J. Immunol. 147:1548 (1991)</p> <p>Valiente et al., Cellular Immunology 145:187 (1992)</p> <p>Trinchieri, Ann. Rev. Immunol., 13:251 (1995)</p> <p>Meager et al., Lancet 350, 1596 (1997)</p> <p>Beeson et al., Ann. NY Acad. Sci. 841:371 (1998)</p> <p>in combination with known methods for creating isolated, recombinant, high-affinity, neutralizing human antibodies, including against human self antigens, and for increasing the affinity of those human antibodies, as set forth, for example in the following:</p> <p>U.S. Patent No. 5,545,807 (Surani et al.)</p> <p>U.S. Patent No. 5,625,126 (Lonberg et al.)</p> <p>U.S. Patent No. 5,770,429 (Lonberg et al.)</p> <p>U.S. Patent No. 6,300,129 (Lonberg et al.)</p> <p>U.S. Patent No. 6,255,458 (Lonberg et al.)</p> <p>U.S. Patent No. 7,084,260 (Lonberg et al.)</p> <p>PCT Publication WO98/24884 (Lonberg et al.)</p> <p>PCT Publication WO97/13852 (Lonberg et al.)</p> <p>PCT Publication WO94/25585 (Lonberg et al.)</p> <p>Lonberg et al., Nature 368:856 (1994)</p> <p>Lonberg et al., Int. Rev. Immunol. 13:65 (1995)</p> <p>Taylor et al., Int. Immunol. 6:579 (1994)</p>
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	Green et al., Nature Genetics 7:12 (1994)
	Wagner et al., Eur. J. Immunol. 24:2672 (1994)
	Wagner et al., Nucl. Acids Res. 22:1389 (1994)
	Harding et al., Ann. NY Acad. Sci. 764:536 (1995)
	Jakobovits, Curr. Op. Biotechnol. 6:561 (1995)
	Bruggemann et al., Immunol. Today 17:391 (1996)
	Fishwild et al., Nature Biotechnology 14:845 (1996)
	Zou et al., FASEB J. 10:1227 (1996)
	Mendez et al., Nature Genetics 15:146 (1997)
	Neuberger et al., Nature 386:25 (1997)
	Bruggemann et al., Curr. Op. Biotechnol.. 8:455 (1997)
	U.S. Patent No. 5,652,138 (Burton et al.)
	U.S. Patent No. 5,804,440 (Burton et al.)
	U.S. Patent No. 5,910,486 (Curiel et al.)
	U.S. Patent No. 6,284,471 (Le et al.)
	U.S. Patent No. 5,919,452 (Le et al.)
	U.S. Patent No. 5,656,272 (Le et al.)
	U.S. Patent No. 5,698,195 (Le et al.)
	U.S. Patent No. 6,277,969 (Le et al.)
	Jespers et al., Nature Biotechnology 12:899 (1994)
	Burton et al. Adv. Immunol. 57:191 (1994)
	Griffiths et al., EMBO J. 13:3245 (1994)
	Vaughan et al., Nature Biotechnology 14:309 (1996)
	Schier et al., J. Mol. Biol. 263:551 (1996)
	Barbas et al., Trends Biotechnol. 14:230 (1996)

	<p>Hoogenboom, Trends Biotechnol. 15:62 (1997)</p> <p>Rader et al., Curr. Op. Biotechnol. 8:503 (1997)</p> <p>Sheets et al., PNAS 95:6157 (1998)</p>
11. The composition of any one of claims 1-4, wherein the antibody, or antigen binding portion thereof, dissociates from the p40 subunit of IL-12 with a K_d of 1×10^{-10} M or less or a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.	Obvious over the same combinations as claim 10 of the 485 patent.
15. A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit, and further comprising an additional agent.	Obvious over the same combinations as claim 1 of the 485 patent.
16. The composition of claim 15, wherein the interleukin comprises a p40 subunit and a p35 subunit.	Obvious over the same combinations as claim 1 of the 485 patent.
17. The composition of claim 16, wherein the interleukin is IL-12.	Obvious over the same combinations as claim 1 of the 485 patent.
18. The position of claim 15, wherein the interleukin comprises a p40 subunit and a p19 subunit.	Obvious over the same combinations as claim 1 of the 485 patent.
19. The composition of any one of claims 15-18 wherein the antibody, or antigen-binding portion thereof, binds to an epitope of the p40 subunit.	Obvious over the same combinations as claim 1 of the 485 patent.
24. The composition of claim 15, wherein the antibody, or antigen binding portion thereof, dissociates from the p40 subunit of the interleukin with a K_d of 1×10^{-10} M or less or a k_{off} rate constant of	Obvious over the same combinations as claim 10 of the 485 patent.

1x10 ⁻³ s ⁻¹ or less, as determined by surface plasmon resonance.	
25. The composition of claim 15, wherein the antibody, or antigen binding portion thereof, neutralizes a biological activity of the interleukin.	Obvious over the same combinations as claim 1 of the 485 patent.
26. The composition of claim 25, wherein the antibody, or antigen binding portion thereof, inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay with an IC ₅₀ of 1x10 ⁻⁹ M or less, or which inhibits human IFN γ production with an IC ₅₀ of 1x10 ⁻¹⁰ M or less.	Obvious over the same combinations as claim 10 of the 485 patent.

The motivation to combine the above references is within the common knowledge of those of ordinary skill in the art, the nature of the problem to be solved, and in the references themselves. A person of ordinary skill in the art would have been motivated to combine the known murine, rat, and human antibodies that bind to IL-12 and/or to the p40 subunit that are described in **U.S. Patent No. 5,811,523 (Trinchieri et al.)**, **U.S. Patent No. 5,780,597 (Gately et al.)**, **U.S. Patent No. 6,054,487 (Sekut et al.)**, **PCT Publication WO98/41232 (Sekut et al.)**, **U.S. Patent No. 6,150,584 (Kucherlapati et al.)**, **U.S. Patent No. 6,673,986 (Kucherlapati et al.)**, **PCT Publication WO94/002602 (Kucherlapati et al.)**, **PCT Publication WO96/33735 (Kucherlapati et al.)**, **PCT Publication WO96/34096 (Kucherlapati et al.)**, **Chizzonite et al., J. Immunol. 147:1548 (1991)**, **Valiente et al., Cellular Immunology 145:187 (1992)**, **Trinchieri, Ann. Rev. Immunol., 13:251 (1995)**, **Meager et al., Lancet 350, 1596 (1997)**, **and/or Beeson et al., Ann. NY Acad. Sci. 841:371 (1998)** with known methods for creating isolated, recombinant, high-affinity, neutralizing human antibodies, including against human self

antigens, and for increasing the affinity of those human antibodies. Those methods include the use of transgenic mouse technology and/or phage display technology, and are described for example in U.S. Patent No. 5,545,807 (Surani et al.), U.S. Patent No. 5,625,126 (Lonberg et al.), U.S. Patent No. 5,770,429 (Lonberg et al.), U.S. Patent No. 6,300,129 (Lonberg et al.), U.S. Patent No. 6,255,458 (Lonberg et al.), U.S. Patent No. 7,084,260 (Lonberg et al.), PCT Publication WO98/24884 (Lonberg et al.), PCT Publication WO97/13852 (Lonberg et al.), PCT Publication WO94/25585 (Lonberg et al.), Lonberg et al., *Nature* 368:856 (1994), Lonberg et al., *Int. Rev. Immunol.* 13:65 (1995), Taylor et al., *Int. Immunol.* 6:579 (1994), Green et al., *Nature Genetics* 7:12 (1994), Wagner et al., *Eur. J. Immunol.* 24:2672 (1994), Wagner et al., *Nucl. Acids Res.* 22:1389 (1994), Harding et al., *Ann. NY Acad. Sci.* 764:536 (1995), Jakobovits, *Curr. Op. Biotechnol.* 6:561 (1995), Bruggemann et al., *Immunol. Today* 17:391 (1996), Fishwild et al., *Nature Biotechnology* 14:845 (1996), Zou et al., *FASEB J.* 10:1227 (1996), Mendez et al., *Nature Genetics* 15:146 (1997), Neuberger et al., *Nature* 386:25 (1997), Bruggemann et al., *Curr. Op. Biotechnol.* 8:455 (1997), U.S. Patent No. 5,652,138 (Burton et al.), U.S. Patent No. 5,804,440 (Burton et al.), U.S. Patent No. 5,910,486 (Curiel et al.), U.S. Patent No. 6,284,471 (Le et al.), U.S. Patent No. 5,919,452 (Le et al.), U.S. Patent No. 5,656,272 (Le et al.), U.S. Patent No. 5,698,195 (Le et al.), U.S. Patent No. 6,277,969 (Le et al.), Jespers et al., *Nature Biotechnology* 12:899 (1994), Burton et al., *Adv. Immunol.* 57:191 (1994), Griffiths et al., *EMBO J.* 13:3245 (1994), Vaughan et al., *Nature Biotechnology* 14:309 (1996), Schier et al., *J. Mol. Biol.* 263:551 (1996), Barbas et al., *Trends Biotechnol.* 14:230 (1996), Hoogenboom, *Trends Biotechnol.* 15:62 (1997), Rader et al., *Curr. Op. Biotechnol.* 8:503 (1997), and/or Sheets et al., *PNAS* 95:6157 (1998). Those methods were known to create recombinant human antibodies having high affinity and

neutralizing activity for human self-antigens. A person of ordinary skill in the art would have been motivated to create human antibodies with the claimed characteristics based on, for example, the common knowledge in the art that IL-12 is important in propagating inflammatory skin lesions. Further, a person of ordinary skill would have been motivated to reduce the immunogenicity of antibodies used for human treatment by, for example, generating human antibodies (*see, e.g.*, U.S. Patent No. 5,530,101 (Queen et al.) at cols. 1-2).

B. Prior Invention

Centocor employees are the prior inventors of the asserted claims of the 128 and 485 patents pursuant to 35 U.S.C. § 102(g)(2). Centocor employees conceived and reduced to practice the alleged invention set forth in the asserted claims prior to the filing dates of the 128 and 485 patents and prior to any earlier date that Abbott may properly rely on for priority, including for the reason that the Abbott inventors suppressed and/or concealed their alleged invention.

The inventors of the 128 and 485 patents suppressed and/or concealed their alleged invention, as evidenced, for example, by their lengthy delay prior to the 1999 filing date of the alleged priority application for the 128 and 485 patents when methods for using their IL-12 antibodies were ready for patenting.

C. Indefiniteness

Claims 1-15, 27-40, 50-64, and 70 of the 128 patent and claims 11 and 24 of the 485 patent are invalid for failing comply with the requirement of 35 U.S.C. § 112 to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Each of those claims recites kinetic properties, including K_d 's and/or rate constants, the values of which depend on the testing methods and conditions used. Those testing methods and conditions

are not adequately set forth in those claims, so that a person of ordinary skill cannot determine the metes and bounds of those claims.

Claims 8-15, 33-40, and 53-63 of the 128 patent and claims 10 and 26 of the 485 patent are invalid for failing comply with the requirement of 35 U.S.C. § 112 to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Each of those claims recites biological properties, including IC_{50} 's, the values of which depend on the testing methods and conditions used. Those testing methods and conditions are not adequately set forth in those claims, so that a person of ordinary skill cannot determine the metes and bounds of those claims.

D. Lack of Written Description

Claims 1-15, 27-40, 50-64, and 70 of the 128 patent and claims 11 and 24 of the 485 patent are invalid for failing to meet the written description requirement. The specifications of the 128 and 485 patents do not provide sufficient description so that a person of ordinary skill would understand that the inventors were in a possession of the claimed invention. For example, the specifications do not describe an accepted method for determining rate constants and/or K_d 's (*see, e.g.*, 128 patent at cols. 116-119; 485 patent at cols. 113-116). Further, the specifications do not evidence that the inventors were in possession of the entire genus of antibodies claimed, including, for example, antibodies made by non-recombinant methods (*see* 128 patent; 485 patent).

E. Lack of Enablement

Claims 1-15, 27-40, 50-64, and 70 of the 128 patent and claims 11 and 24 of the 485 patent are invalid for failing to meet the enablement requirement. The specifications of the 128 and 485 patents do not enable the full scope of the claimed invention. For example, the

specifications do not teach an accepted method for determining rate constants and/or K_d 's (*see, e.g.*, 128 patent at cols. 116-119; 485 patent at cols. 113-116). Further, the specifications do not provide sufficient description to enable one skilled in the art to make the full scope of the invention as claimed, including, for example, antibodies made by non-recombinant methods (*see* 128 patent; 485 patent).

II. Preliminary Non-Infringement Contentions

Centocor does not infringe any of the asserted claims, because the accused product Stelara™ does not contain each and every limitation of the asserted claims either literally or under the doctrine of equivalents.

First, the accused product does not meet the K_d or rate constant elements as set forth in claims 1-15, 27-40, 50-64, and 70 of the 128 patent and claims 11 and 24 of the 485 patent (*see, e.g.*, **Exhibit O** to Abbott's May 10, 2010 Supplemental Preliminary Infringement Contentions).

Second, the accused product does not meet the IC_{50} elements set forth in claims 8-15, 33-40, and 53-63 of the 128 patent and claims 10 and 26 of the 485 patent (*see, e.g.*, **Exhibit P** to Abbott's May 10, 2010 Supplemental Preliminary Infringement Contentions).

Third, the accused product does not comprise an additional agent as set forth in claims 1-4, 6-11, 15-19, and 24-26 of the 485 patent (*see, e.g.*, 485 patent at cols. 68-70, 72; **Exhibit B** to Abbott's May 10, 2010 Supplemental Preliminary Infringement Contentions).

Date: July 19, 2010

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CERTIFICATE OF SERVICE

I certify that, on July 19, 2010, this document (filed through the ECF system) will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF).

/s/ Matthew A. Pearson